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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/016,604 | 12/07/2001 | Pablo D. Garcia | PP016466.0002 | 6543 |

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| EXAMINER | |
|---|---|
| HUMPHREY, LOUISE WANG ZHIYING | |
| ART UNIT | PAPER NUMBER |
| 1648 | |

| MAIL DATE | DELIVERY MODE |
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| 03/04/2009 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/016,604 | GARCIA ET AL. | |
| | Examiner | Art Unit | |
| | LOUISE HUMPHREY | 1648 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *20 November 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *77-87* is/are pending in the application.

4a) Of the above claim(s) *80-82* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *77-79 and 83-87* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/2/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

This Office Action is in response to the amendment filed 20 November 2008. Claims 1-76 and 88-113 have been cancelled. Claims 77-87 are pending. Claims 80-82 are withdrawn as being directed to a nonelected sequence. Claims 77-79 and 83-87 are currently examined.

### *Information Disclosure Statement*

The information disclosure statement (IDS) submitted on 11 February 2009 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner. The dated and signed 1449 form is attached.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. §112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of claims 1, 3, 10, 13-15, 39-49, 53-65, 69-79, 83-90, 94-99, 103-108, 112 and 113 under 35 U.S.C. §112, second paragraph, as being indefinite is withdrawn in response to the Applicants' amendment or cancellation of the claims.

The rejection of claims 1,3, 10, 13-15, 39-49, 53-65, 69-79, 83-90, 94-99, 103-108, 112 and 113 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification commensurate in scope is withdrawn in response to Applicants' amendment or cancellation of the claims.

However, upon further consideration, the withdrawn scope of enablement rejection is replaced by the following new ground of rejection:

Claims 77, 78 and 83-87 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for assaying, in a patient prostate sample, the RNA of HERV-K(CH) that is at least 150% relative to a control sample level, does not reasonably provide enablement for (a) assaying, in a patient prostate or blood sample, the polypeptide of HERV-K(CH) that is at least 150% relative to a control sample level; or (b) assaying, in a patient blood sample, the RNA of HERV-K(CH) that is at least 150% relative to a control sample level. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In making a determination as to whether an application has met the requirements for enablement under 35 U.S.C. 112 ¶ 1, the courts have put forth a series of factors (MPEP §2164.01(a)). See, *In re Wands*, 8 USPQ2d 1400, at 1404 (CAFC 1988); and *Ex Parte Forman*, 230 U.S.P.Q. 546 (BPAI 1986). The factors that may be considered include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the

predictability or unpredictability of the art, and (8) the breadth of the claims. *Id.* While it is not essential that every factor be examined in detail, those factors deemed most relevant should be considered.

The instant claims are directed to screening all expression products, including RNA and protein, of a human endogenous MMTV-like subgroup 2 (HML-2) retrovirus and detecting at least 150% increased level of both RNA and protein level in a patient prostate or blood sample to determine the presence of prostate cancer.

The guidance in the specification is limited to assaying both RNA and polypeptide expression products of these viruses in prostate cells and assaying polypeptide in blood cells (page 24, line 23 to page 25, line 9). However, the specification does not provide guidance on how to assay for RNA in blood samples. Furthermore, the specification only contains data for at least 150% elevated RNA level in prostate cells but not blood cells. Neither does the specification show whether the level of mRNA expression is correlated to the level of protein expression in blood and prostate cells.

It is known in the art that expression levels of mRNA and protein by cell types exhibit a range of correlations for different genes (Pascal, 2008). Immunostaining and microarray analysis are powerful tools for determining gene and protein expression patterns. However, it has been problematic to establish agreement between semi-quantitative immunostaining data and gene array data obtained from tissue specimens in order to determine a direct relationship between protein and mRNA levels (Pascal, 2008). Pascal *et al.* (2008) report that the correlation of expression levels was poor to

moderate in the prostate while Chen *et al.* report a lack of correlation for mRNA and protein expression in lung tumor cells (Chen, 2002) and Lichtinghagen *et al.* (2002) report different mRNA and protein expression in benign and malignant prostate tissue. Given the high level of unpredictability, it is uncertain whether the at least 150% elevated mRNA expression level the applicants observed in prostate cells is predictive for at least 150% elevated mRNA expression level in other sample cells such as blood or is predictive for at least 150% elevated protein expression in prostate or blood samples.

The working example indicates at least 150% increased RNA expression in prostate tissue. However, the working example neither shows concordant protein expression in prostate or blood sample, nor shows the same amount of increased RNA expression in blood sample. Therefore, the instant specification and the working example do not address the problem of discordance between RNA and protein expression in various cell types.

At the time the invention was made, no one has made a clear-cut showing of quantitative correlation between the RNA and protein expression levels in various cell types. It is highly unpredictable whether the skilled artisan would observe the same 150% elevated RNA expression in blood samples as Applicants measured in the prostate tumor cells. It is even more unpredictable whether the skilled artisan would detect more than 150% elevated protein expression in all cell types. Thus, the validity of the number, 150%, in the expression level of both RNA and protein in all cell types as an indication of prostate cancer remains questionable.

Applicant's specification does not address these factors and does not disclose that the instant invention has overcome these problems. Therefore, it would require undue and unpredictable experimentation for one skilled in the art to use the claimed method.

Applicants have not provided sufficient guidance to allow one skilled in the art to practice the claimed invention with a reasonable expectation of success and without undue experimentation. In the absence of such guidance and evidence, the specification fails to provide an enabling disclosure. A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993).

***Correspondence***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louise Humphrey whose telephone number is 571-272-5543. The examiner can normally be reached on Mon-Fri, 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell, can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/L. H./
Examiner, Art Unit 1648

/Jeffrey S. Parkin/
Primary Examiner, Art Unit 1648

13 February 2009